

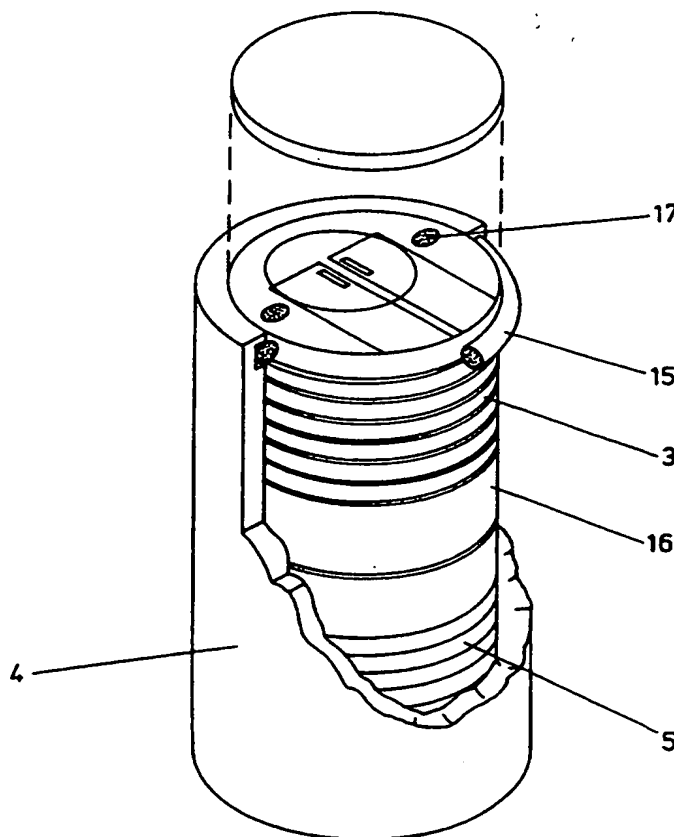


## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>5</sup> :</b>  <b>G01N 27/28, 35/00, 33/487</b>	<b>A1</b>	<b>(11) International Publication Number:</b> <b>WO 94/10558</b>  <b>(43) International Publication Date:</b> 11 May 1994 (11.05.94)
<b>(21) International Application Number:</b> PCT/GB93/02241 <b>(22) International Filing Date:</b> 1 November 1993 (01.11.93)  <b>(30) Priority data:</b> 9223016.8                      3 November 1992 (03.11.92)    GB  <b>(71) Applicant (for all designated States except US):</b> ENVI- ROMED PLC [GB/GB]; 130 Brixton Hill, London SW2 1RS (GB).  <b>(72) Inventors; and</b> <b>(75) Inventors/Applicants (for US only) :</b> FRIEDLANDER, Uri [GB/GB]; 20 Belsize Avenue, London NW3 4AU (GB). HIGGINS, Irving, John [GB/GB]; Cotswold Graze Hill, Ravensden, Bedford MK44 2TF (GB). D'COSTA, Eric [GB/GB]; 5 Wordsworth Avenue, Newport Pagnell, Bucks MK16 8RT (GB). HALL, Geoffrey, Frank [GB/ GB]; 4 Partridge Piece, Cranfield, Bedfordshire MK43 0BP (GB). MORRIS, Nicholas [GB/GB]; 71 Spring Road, Kempston, Bedfordshire MK42 8LT (GB).		<b>(74) Agent:</b> BROWNE, Robin, Forsythe; Urquhart-Dykes & Lord, Tower House, Merrion Way, Leeds LS2 8PA (GB).  <b>(81) Designated States:</b> AU, CA, JP, US, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the</i> <i>claims and to be republished in the event of the receipt of</i> <i>amendments.</i>

**(54) Title:** ELECTROCHEMICAL SENSOR**(57) Abstract**

An electrochemical sensor comprises a housing and a polarity of disposable test elements (3) located in the housing and arranged so that the elements are presented sequentially to a test station, wherein the electrodes may be contacted with a specimen containing an analyte, the test station further including electrical contact means adapted to engage said electrode element to produce a signal characteristic of the analyte.



**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GB	United Kingdom	MR	Mauritania
AU	Australia	GE	Georgia	MW	Malawi
BB	Barbados	GN	Guinea	NE	Niger
BE	Belgium	GR	Greece	NL	Netherlands
BF	Burkina Faso	HU	Hungary	NO	Norway
BG	Bulgaria	IE	Ireland	NZ	New Zealand
BJ	Benin	IT	Italy	PL	Poland
BR	Brazil	JP	Japan	PT	Portugal
BY	Belarus	KE	Kenya	RO	Romania
CA	Canada	KG	Kyrgyzstan	RU	Russian Federation
CF	Central African Republic	KP	Democratic People's Republic of Korea	SD	Sudan
CG	Congo	KR	Republic of Korea	SE	Sweden
CH	Switzerland	KZ	Kazakhstan	SI	Slovenia
CI	Côte d'Ivoire	LI	Liechtenstein	SK	Slovakia
CM	Cameroon	LK	Sri Lanka	SN	Senegal
CN	China	LU	Luxembourg	TD	Chad
CS	Czechoslovakia	LV	Latvia	TC	Togo
CZ	Czech Republic	MC	Monaco	TJ	Tajikistan
DE	Germany	MD	Republic of Moldova	TT	Trinidad and Tobago
DK	Denmark	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	US	United States of America
FI	Finland	MN	Mongolia	UZ	Uzbekistan
FR	France			VN	Viet Nam
GA	Gabon				

-1-

## ELECTROCHEMICAL SENSOR

This invention relates to an electrochemical sensor of the kind incorporating a plurality of disposable electrodes contained within a housing. The invention relates particularly but not exclusively to sensors wherein the electrodes incorporate an immobilised enzyme for assay of biological analytes.

Suitable electrodes may be manufactured by absorption or deposition of palladium or platinum onto carbon particles which may subsequently be incorporated in a porous self supporting structure. Alternatively a substrate composed of for example carbon paper or carbon cloth may be employed. The manufacture and properties of such electrodes is disclosed in US-A-4044193, US-A-4166143, US-A-4293396 and US-A-4476696. Alternative constructions of electrodes may be employed. The electrode surface may be plated with a mercury film. A mixture of enzyme, carbon and mediator species may be deposited on the electrode surface to form an enzyme electrode. The electrode may also incorporate a membrane containing mediator according to PCT/GB91/01444.

According to the present invention an electrochemical sensor comprises a housing and a plurality of disposable electrode elements located in the housing and arranged so that said electrode elements may be presented sequentially in use to a test station wherein the electrodes may be contacted with a specimen containing an analyte, the test station further including electrical contact means adapted to engage said electrode element to produce a signal characteristic of said analyte.

The signal may be indicative of the present, absence or concentration of the analyte.

The sensor may include a display adapted to provide a visible, audible or other indication in response to said signal. A liquid crystal display may provide a visible measure of the concentration of the analyte or may indicate whether a particular threshold has been attained.

-2-

Each electrode preferably comprises a laminar member having a working surface carrying the immobilised reagents and an impermeable substrate. Liquid applied to the working surface is supported thereon for analysis and is prevented from drainage of the electrode to contaminate an adjacent unused electrode element.

The test station preferably comprises a receptacle for a liquid specimen. A receptacle may incorporate an aperture communicating with the working surface of the electrode when the latter is engaged with the test station. In preferred embodiments of the invention the receptacle comprises a plate having said aperture for reception of a liquid specimen.

In preferred embodiments of the invention a multiplicity of electrode elements are arranged in stacked relationship in a magazine, the first electrode element engaging said receptacle at the test station to form an impermeable seal preventing a liquid specimen from contacting the second subsequent electrode. The stack of electrodes is preferably biased towards the receptacle for example by means of a spring.

The electrodes may be circular, rectangular, elliptical, polygonal or otherwise shaped. Means is preferably provided to ensure that the electrodes are correctly oriented with respect to the electrical contacts on the test station. This may comprise engagement of surfaces of the electrode element with corresponding formations of the housing.

The magazine is preferably moveable within the housing, being urged in use towards the receptacle to form a liquid-proof seal. In preferred aspects of the invention an ejector is provided to displace spent electrode elements from the test station. The ejector may comprise a laminar member slidable between first position wherein an element is located at the test station and a second position wherein the element is ejected from the apparatus. A linearly slidable ejector may be provided. Alternatively a rotatable configuration, in the manner of a daisy wheel may be employed.

The magazine may be closable with a removable top, for

-3-

example connected to the magazine by means of a screw thread. The ejector is preferably arranged to disengage the top and magazine prior to ejection of the element. In a first preferred embodiment the top may be screwed from the magazine and in a second preferred embodiment the magazine may be unscrewed from the fixed top. An overcentre sprung arrangement may facilitate movement of the ejector between a position wherein the element is disposed in the magazine with the top seals and a second position wherein the element is deployed at the test station. Upon further actuation the ejector returns to the original position and the used element is ejected.

The invention finds particular application in completed analysis of biological fluids, for example blood glucose, alcohol in saliva or urine analysis. The invention also finds use in environmental analysis, for example analysis for ammonia, chlorine, phenols and heavy metals especially lead, copper, zinc, cadmium and mercury, in river water, industrial effluent or other aqueous samples.

The invention is further described by means of example but not in any limitative sense with reference to the accompanying drawings of which:

Figure 1 is an exploded view of the components of a sensor in accordance with the invention;

Figure 2 illustrates the assembled sensor;

Figure 3 is a partially cut away detailed view of the sensor;

Figure 4 is a cross-sectional view illustrating use of the ejector arrangement; and

Figures 5 and 6 are cross-sectional views of alternative arrangements.

The arrangement shown in Figure 1 comprises a plate 1 having a dish-like receptacle 2 communicating with the lower surface of the plate 1 by means of aperture. A plurality of laminar disc-like electrode elements 3 is arranged in overlying stacked relation within a tubular magazine 4. The stack of electrodes 3 is urged upwardly against the lower surface of the plate 1 by means of a first spring 5. A second larger spring

-4-

6 bears against the tubular magazine 4 and urges the latter into engagement with the plate 1. An outer tube 7 and plug 8 serve to retain the spring loaded arrangement in the correct configuration.

Figure 2 illustrates an example of a sensor in accordance with this invention. A body 10 incorporating an LED display 11 is adapted to conform to a users hand. The receptacle 13 is arranged to receive a liquid specimen and an ejector 12 is arranged when manually actuated to discharge a spent electrode element. Operation of the sensor is described below.

The arrangement shown in Figure 3 includes an upper portion of the inner tube 4 including a sealing ring 15 arranged to prevent ingress of liquid into the stack of unused elements 3. A desiccant disc 16 disposed below the stack of elements 3 serves to maintain the latter in an anhydrous environment. The compression spring 5 bears against the lower surface of the desiccant disc urging the uppermost electrode element into contact with the receptacle at the test station. When circular electrode elements are employed locating means 17 extending lengthwise to the stack of electrodes serves to maintain the stack in the correct orientation with respect to electrical contacts disposed on the lower surface of the plate 1. In alternative embodiments of the invention the electrode elements may be rectangular or otherwise shaped to prevent disorientation of them within the magazine.

Use of the apparatus is described with reference to Figures 4a, b and c. In Figure 4a a stack of electrode elements 30 and desiccant disc 27 are urged upwardly by a spring 25 into engagement with the lower surface of a plate 20 having an aperture 21 to which a liquid specimen 22 may be applied. The upper disc 28 of the stack is sealed at the test station by an O ring 29 carried by the magazine 23. The magazine 23 is urged by compression spring 26 into engagement with the lower surface of the plate 20. The lower surface of the plate 20 carries electrical contacts (not shown) adapted to connect to the electrodes on the electrode element 28 at the

-5-

test station. Electrochemical reaction with the analyte specimen 22 produces an electrical signal and provides a visible display in conventional manner.

Figure 4b illustrates the first stage of ejection of a spent electrode 28 from the test station. The magazine 23 is withdrawn against the pressure of the compression spring 26, for example by means of a manual actuator (not shown). An ejector 31 shown in Figure 4c may then be used to displace the element 28 from the test station. Withdrawal of the ejector 31 allows the magazine 23 to return to the position shown in Figure 4a and a fresh electrode element is available for use.

In alternative embodiments of the invention the elements 30 may be disposed in side by side relation rather than in a stack 30. The elements may be mounted on a flexible support member, for example on a strip of release paper. Alternatively the elements 30 may be supplied to the test station by a daisy wheel arrangement.

Figure 5 shows an alternative arrangement wherein the sensor stack 31 is held within a cartridge 32 having a screw top 33 sealed with an O ring 34. This provides airtight storage for the sensors when not in use. The sensors are arranged to be delivered from the cartridge by turning the screw top 33. Turning the top 33 raises the top on the thread sufficiently to allow a pusher 35 to push the top electrode sensor from the stack into test position 36. The pusher 35 may be driven by the turning action of the screw top 33 via a pusher gear mechanism 37. The pusher 35 is retracted and the screw top 33 is closed by the action of a coil spring 38. In this arrangement the sensor is dispensed from the sealed cartridge automatically upon the rotation of the cap, and the cap closes, sealing the cartridge when manual pressure is released.

Figure 6 shows a further embodiment wherein the pusher 40 is coupled with a two position spring 41 that allows the pusher to rest in either of two positions in an overcentre manner. The sensor cartridge for magazine 42 carries a stack of sensors 43 and a spring 44 maintains an upward pressure on the stack

-6-

43. The first action of the pusher 40 is to lift the cartridge top 45 from the seal 46 to a sufficient distance to allow the uppermost sensor to be pushed into the test position 47. In an alternatively embodiment of the invention the initial action of the pusher causes the body of the cartridge 42 to be lowered a sufficient distance to allow the uppermost sensor to be pushed into the test station 47. In such an arrangement the cartridge top can be fixed and can become a non-disposable component of the apparatus, the magazine being <sup>re-</sup>placable when the supply of electrode elements is exhausted.

The electrode elements may incorporate reagents allowing enzyme assay of alcohol, glucose or other metabolites. Alternatively immunoassay agents may be provided, for example as disclosed in EP 0424586.



-7-

## CLAIMS

1. An electro-chemical sensor comprising a housing and a plurality of disposable electrode elements located in the housing and arranged so that said electrodes may be presented sequentially in use to a test station wherein the electrodes may be contacted with a specimen containing an analyte, the test station further including electrical contact means adapted to engage said electrode elements to produce a signal characteristic of said analyte.

2. A sensor as claimed in claim 1, wherein the signal is indicative of the presence, absence or concentration of the analyte.

3. A sensor as claimed in any preceding claim, wherein the display is adapted to provide a visible, audible or other indication in response to said signal.

4. A sensor as claimed in any preceding claim wherein said electrode comprises a laminar member having a working surface carrying immobilised reagents and an impermeable substrate.

5. A sensor as claimed in any preceding claim wherein the test station includes a receptacle for a liquid specimen.

6. A sensor as claimed in claim 5, wherein the receptacle comprises an aperture communicating with the working surface of the electrode when the latter is engaged with the test station.

7. A sensor as claimed in any preceding claim, wherein a multiplicity of electrode elements are arranged in stacked relationship in a magazine, the a electrode element being engaged at the test station to cooperate with the receptacle to form an impermeable seal.

8. A sensor as claimed in claim 7, including locator means to ensure that the electrodes are correctly oriented with respect to the test station.

9. A sensor as claimed in claim 7 or 8, wherein the magazine is moveable within the housing, being urged in use towards the receptacle to form an impermeable seal.

10. A sensor as claimed in any preceding claim,

-8-

including an ejector adapted to displace spent electrode elements from the test station.

11. A sensor as claimed in claim 10, wherein the ejector comprises a laminar member slidable between a first position wherein an element is located at the test station and a second position wherein the element is ejected from the apparatus.

12. A sensor as claimed in claim 11, including a linearly slidable ejector.

13. A sensor as claimed in claim 7 or any claim appendant on claim 7, wherein the magazine includes a sealable top.

14. A sensor as claimed in claim 13 wherein the magazine is sealable with a screw top.

15. A sensor as claimed in claim 13 or 14, wherein actuation of the top causes an electrode element to be presented to the test station.

16. A sensor as claimed in claim 15, wherein the top is arranged to reseal the magazine when manual pressure is released after presentation of the element to the test station.

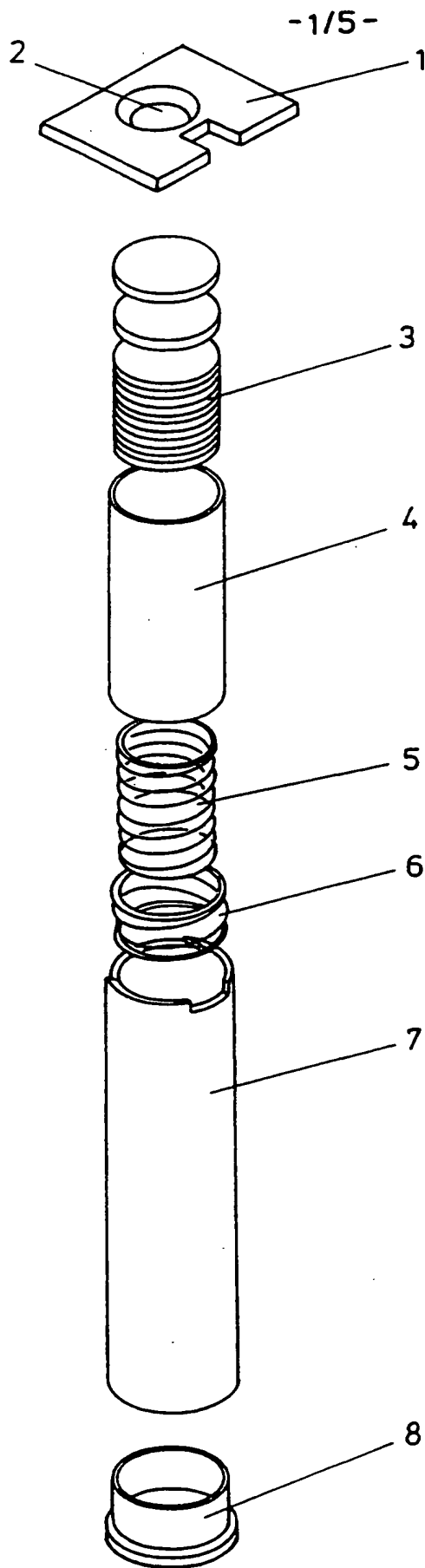


FIG. 1

- 2/5 -

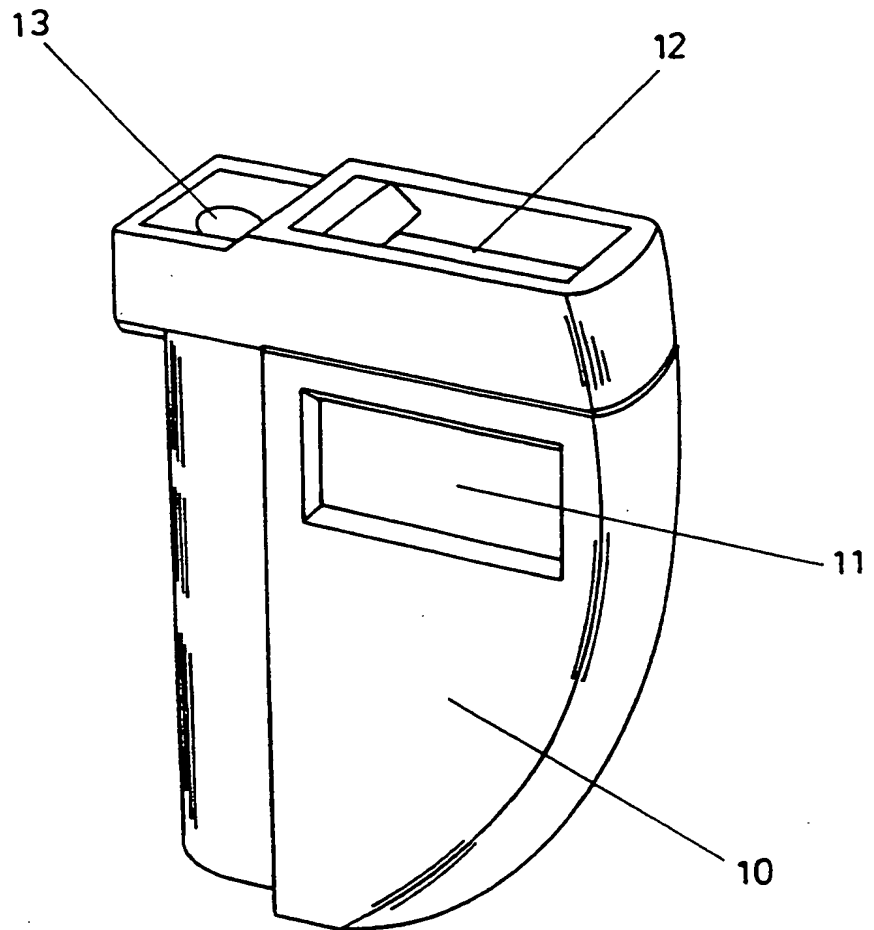


FIG. 2

- 3/5 -

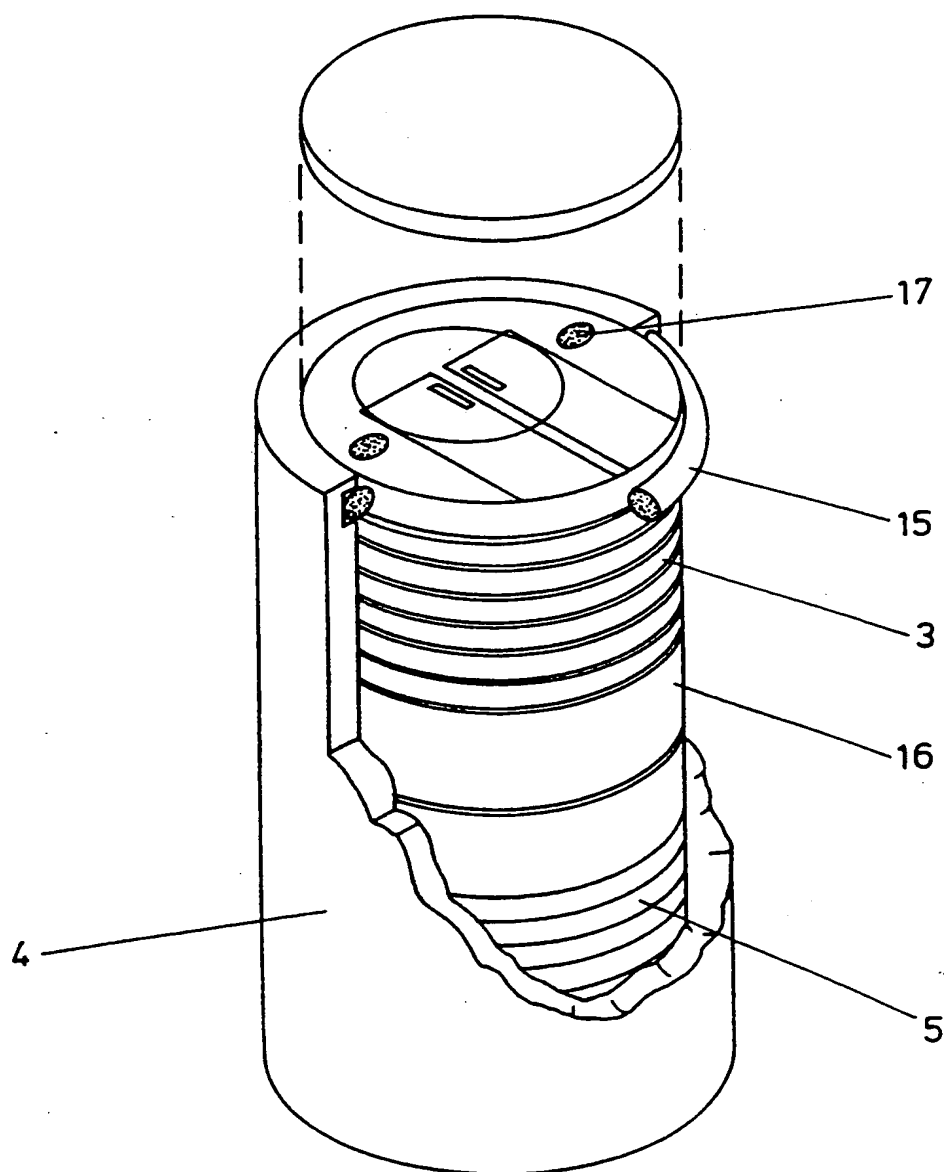
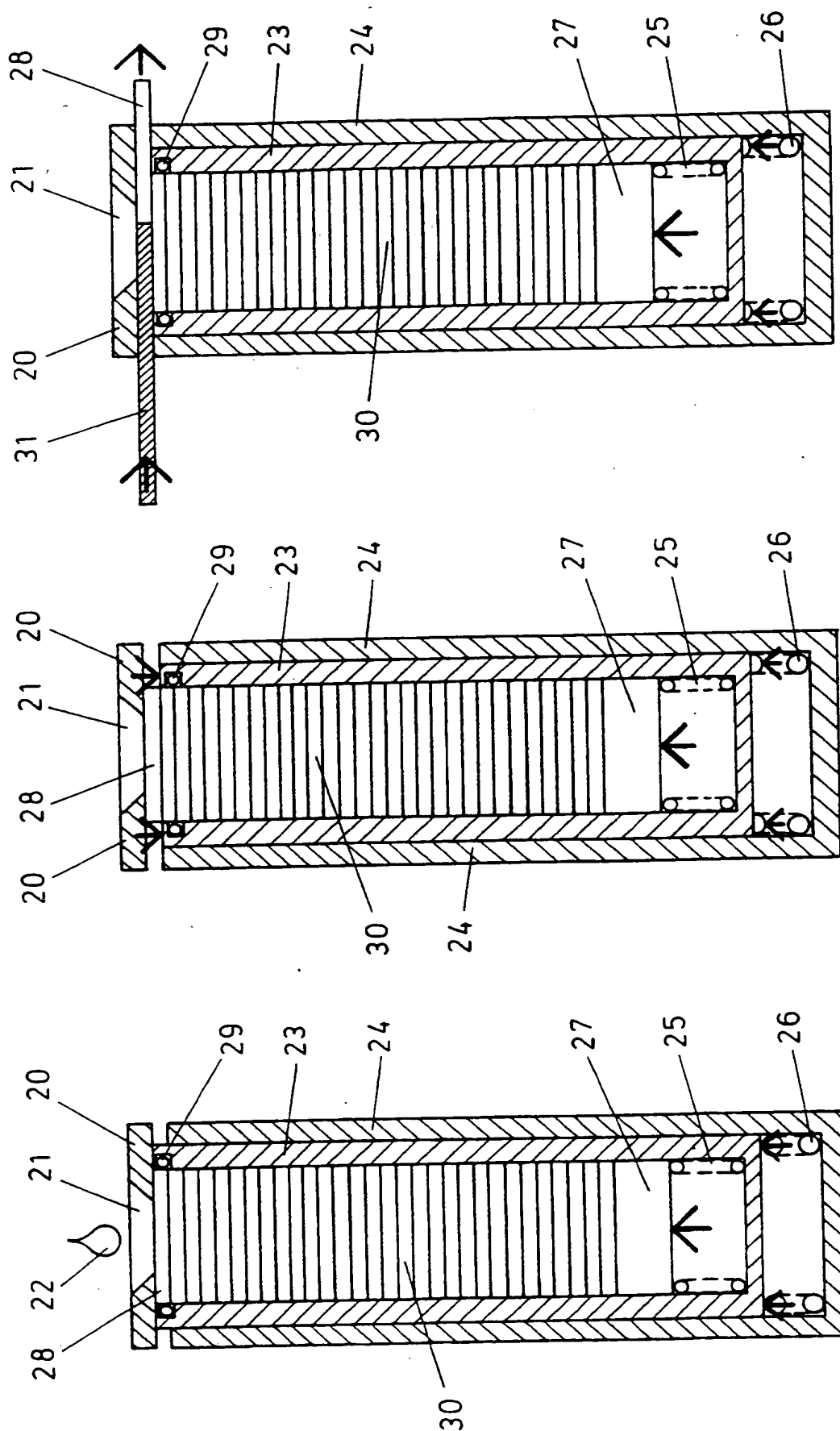


FIG. 3

**SUBSTITUTE SHEET**

-4/5-



(c)

(b)

(a)

FIG. 4

- 5/5 -

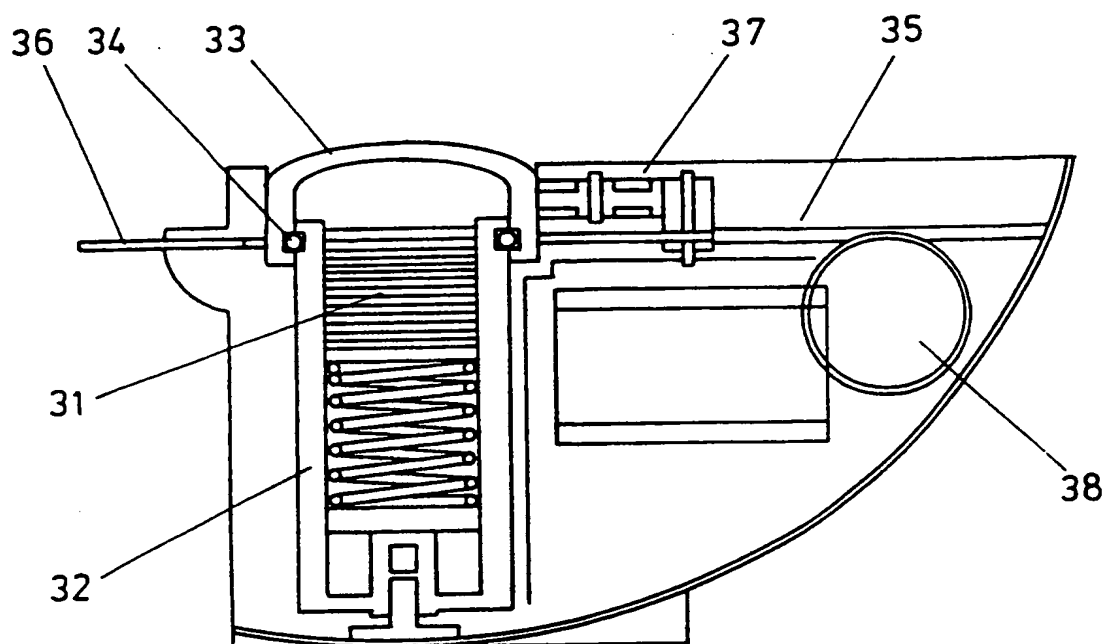


FIG. 5

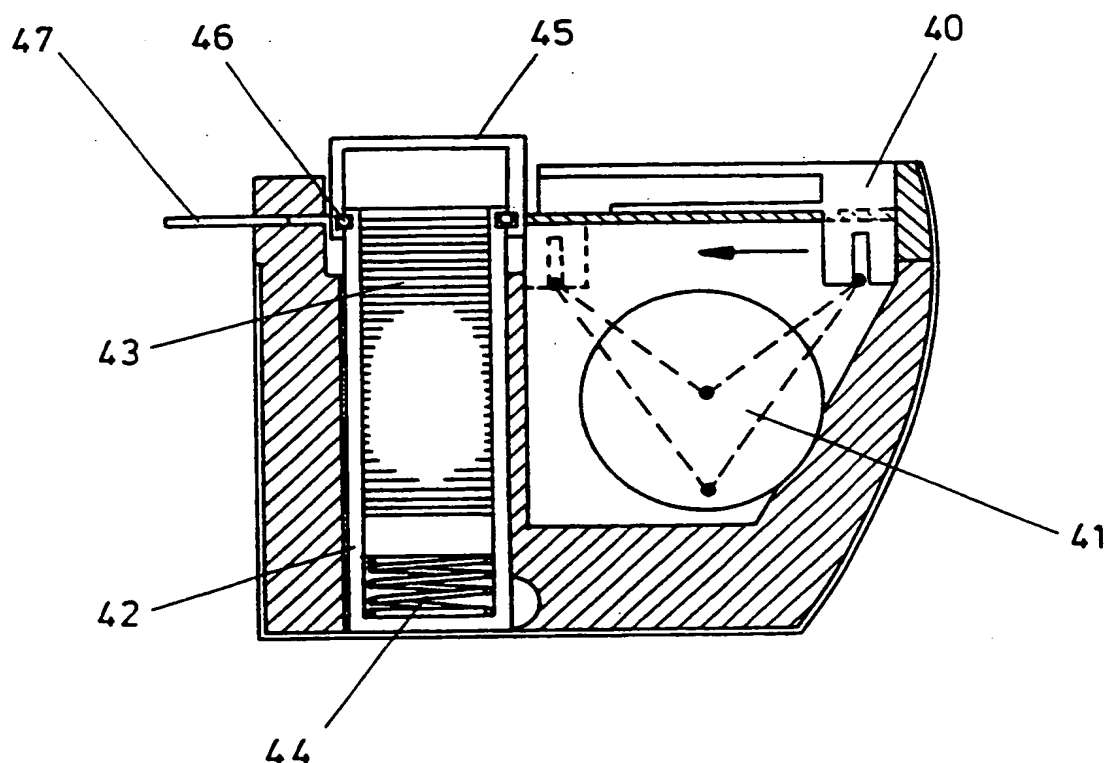


FIG. 6

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 93/02241

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 5 G01N27/28 G01N35/00 G01N33/487

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 5 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB,A,2 001 443 (EASTMAN KODAK COMPANY) 31 January 1979	1-3
A	see the whole document ---	4-16
A	US,A,5 030 418 (MIYATA) 9 July 1991 see the whole document -----	1-16



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

18 February 1994

Date of mailing of the international search report

03.03.94

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+31-70) 340-3016

Authorized officer

Bosma, R